Effects of Toxic Metals on Learning Ability and Behavior

Bernard Windham (Ed.)

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1.1 Mechanisms of Developmental Damage by Toxic Metals

The human brain forms and develops over a long period of time compared to other organs, with neuron proliferation and migration continuing in the postnatal period. The blood-brain barrier is not fully developed until the middle of the first year of life. Similarly there is postnatal activity in the development of neuronal receptors and transmitter systems, as well as in the production of myelin. The fetus has been found to get significant exposure to toxic substances through maternal blood and across the placenta, with fetal levels of toxic metals often being higher than that of maternal blood (19, 30-32, 41, 42, 169b). Likewise infants have been found to get significant exposure to toxics, such as mercury and organochlorine compounds that their mother is exposed to, through breast-feeding (26, 30-32, 101, 107, 169b). Other toxic exposures are also extremely common as documented in Section 1.4.

The incidence of neurotoxic or immune reactive conditions such as autism, schizophrenia, ADD, dyslexia, learning disabilities, etc. have been increasing rapidly in recent years (2, 80-82, 113-115, 143, 144, 149, 169). A recent report by the National Research Council found that 50% of all pregnancies in the U.S. are now resulting in prenatal or postnatal mortality, significant birth defects, developmental neurological problems, or otherwise chronically unhealthy babies (82). There has been a similar sharp increase in developmental conditions in Canadian children (132), including increases in learning disabilities and behavioral problems, asthma and allergies, and childhood cancer. Not all children are equally affected by a given level of toxic exposures, and *susceptibility factors*[1] such as immune reactivity, genetic factors affecting ability to excrete toxic metals, and other toxic exposures have major influences on toxicity effects.

A 2009 study found that inorganic mercury levels in people have been increasing rapidly in recent years (177). It used data from the U.S. Centers for Disease Control and Prevention's National Health Nutrition Examination Survey (NHANES) finding that while inorganic mercury was detected in the blood of 2 percent of women aged 18 to 49 in the 1999-2000 NHANES survey, that level rose to 30 percent of women by 2005-2006. Surveys in all states using hair tests have found dangerous levels of

[1]**Informativo:** "Susceptibility Factors in Mercury Toxicity: Immune Reactivity, Detoxification System Function, Enzymatic Blockages, Synergistic Exposures".

mercury in an average of 22% of the population, with over 30% in some states like Florida and New York (178).

Studies and clinical experience at treatment clinics have found consistently that gastrointestinal, immunologic and metabolic problems are found in children with ADHD, that are related to prenatal and neonatal exposure to toxic substances with much of these being related to vaccinations. (173) Lower GI dysfunction, enzyme deficiencies and impairments of hepatic detoxification pathways are very common. Many ADHD/autism patients have "leaky gut" syndrome, and inability to digest wheat gluten and milk casein, resulting in neurotoxic substances being dumped in the blood with significant adverse behavioral impacts.

Exposure to toxic chemicals or environmental factors appear to be a factor in at least 28 percent of the 4 million U.S. children born each year (6-23), with at least 1 in 6 having one of the neurological conditions previously listed according to the U.S. Census Bureau (82c). U.S. EPA estimates that over 3 million of these are related to lead or mercury toxicity, with approximately 25% of U.S. kids getting mercury exposure at dangerous levels (2, 41, 81, 108). Evidence indicates that over 60,000 children are born each year with neurodevelopmental impairment due to methyl mercury (107, 2), with even higher levels of exposure and impairment from two other sources, vaccines and mother's amalgam dental fillings (81, 169ab).

1.2 Extent of exposure of children to toxic metals

The U.S. Center for Disease Control ranks toxic metals as the number one environmental health threat to children, adversely affecting large numbers of children in the U.S. each year and thousands in Florida (1-4, 108). According to an EPA/ATSDR assessment, the toxic metals lead, mercury, and arsenic are the top 3 toxics having the most adverse health effects on the public based on toxicity and current exposure levels in the U.S. (1), with cadmium, chromium and nickel also highly listed. According to the American Academy of Child and Adolescent Psychiatry, an estimated one out of every 6 children in the U.S. have blood levels of lead in the toxic range (87), and studies estimate that over 12 million children suffer from learning, developmental, and behavioral disabilities including ADD, autism, schizophrenia, and mental retardation (87, 82, 42, 113, 149, 157). Large numbers of people have been found to have allergic conditions and immune reactive autoimmune conditions due to the toxic metals, especially inorganic mercury and nickel (28, 29, 59). These metals have also been found to diminish the cellular ATP energy function and be related to chronic fatigue 28, 29, 59, 170). One of the mechanisms documented is causing intestinal dysbiosis resulting in poor vitamin and mineral absorption (112) and *"leaky gut"*[2].

The level of exposure in most infants to mercury thimerosal has been found to be many times higher than the federal limits for mercury exposure (81, 122, 169). The largest increase in neurological problems has been in infants (2, 80-82), with an increase in autism cases to over 500,000 (2, 80-82, 169), an over 500% increase to a level of almost 1 per 300 infants in the last decade (80), making it the 3rd most common chronic childhood condition, along with similar increases in ADD (2, 41, 83, 88, 143, 149, 169a, 172). According to the American Academy of Pediatrics between 4 to 12% of all school age children are affected by ADHD (144) and a similar number have some degree of dyslexia (41). However large surveys of elementary level student records finds much higher levels - with over 20% of elementary school boys in some areas being treated for ADD (143). Similar levels of children have been found to have mood or anxiety disorders. At least 4% of adults have also been found to have ADHD symptoms (176). Studies have found that long term use of stimulant drugs commonly are not effective in the long run and causes significant adverse neurological and health effects (145, 172), There are more effective options available to deal with such conditions without such adverse effects including dealing with the underlying causes (172, 173, 175, 176) and diet, exercise, and

[2] **Internet:** "http://www.flcv.com/leakyghg.html".

supplement options that deal with underlying deficiencies (172).

The heavy metals (lead, mercury, cadmium, nickel) tend to concentrate in the air and in the food chain along with other toxic metals like and aluminum, facilitating metal poisoning which is the most widespread environmental disorder in the U.S (1-4, 34). Mercury and cadmium from combustion emissions are also accumulating in coastal estuaries and inland water body sediments, and are widespread in shellfish and other org anisms (34-36). Mercury and cadmium are extremely toxic at very low levels and have serious impacts on the organisms in water bodies that accumulate them (34, 2). These heavy metals have also been found to be endocrine system disrupting chemicals and have been found to be having effects on the endocrine and reproductive systems of fish, animals, and people, similar to the reproductive and developmental effects of organochlorine chemicals (30, 33, 155, 170). Estrogenic chemicals like mercury have been found in Florida wildlife at levels that feminized males to the extent of not being able to reproduce, and also had adverse effects on the female reproductive systems (33, 36). Similar effects have also been documented in humans (33, 37, 155, 170).

1.3 Developmental effects of toxic metals on cognitive ability and behavior

Studies have found that heavy metals such as mercury, cadmium, lead, aluminum, and tin affect chemical synaptic transmission in the brain and the peripheral and central nervous system (19, 24, 25, 37-40, 57, 154, 169, 170). They also have been found to disrupt brain and cellular calcium levels that significantly affect many body functions: such as (a) calcium levels in the brain affecting cognitive development and degenerative CNS diseases (5, 28, 170, 74) (b) calcium-dependent neurotransmitter release which results in depressed levels of serotonin, norepinephrine, and acetylcholine (5, 19, 28, 44-47, 83, 110, 170) - related to mood and motivation; (c) cellular calcium-sodium ATP pump processes affecting cellular nutrition and energy production processes (5, 28, 170); (d) calcium levels in bones causing skeletal osteodystery (5, 74) . Toxic metals have also been found to affect cellular transfer and levels of other important minerals and nutrients that have significant neurological and health effects such as magnesium, lithium, zinc, iron, Vitamins B-6 & B1-12 (5, 27, 46, 68, 75, 83, 104, 160-163, 170, 170). Based on thousands of hair tests, at least 20% of Americans are deficient in magnesium and lithium (5, 68, 76, 83), with zinc deficiencies also common (123, 160, 163) and iron deficiencies (162). The resulting deficiency of such essential nutrients has been shown to increase toxic metal neurological damage (5, 74, 75, 83, 160, 170). Cerebrospinal magnesium was found to be significantly lower in both depression and adjustment disorder and in those who have attempted suicide (166).

Much of the developmental effects of mercury (and other toxic metals) are due to prenatal and neonatal exposures damage to the developing endocrine (hormonal) system (155, 169, 32c). A recent study found that prenatal Hg exposure is correlated with lower scores in neurodevelopmental screening, but more so in the linguistic pathway (32c). Prenatal and neonatal toxic metal exposure to mercury, lead, arsenic, cadmium, nickel, and aluminum have been documented in medical publications and medical texts to cause common and widespread neurological and psychological effects including depression, anxiety, obsessive compulsive disorders, social deficits, other mood disorders, schizophrenia, anorexia, cognitive impairments, ADHD, autism, seizures, etc. (48, 113-115, 153-155, 157, 169, 170). Children with autism had significantly (2.1-fold) higher levels of mercury in baby teeth, but similar levels of lead and similar levels of zinc. Children with autism also had significantly higher usage of oral antibiotics during their first 12 mo of life. Baby teeth are a good measure of cumulative exposure to toxic metals during fetal development and early infancy (168).

Studies have also found heavy metals to deplete glutathione and bind to protein-bound sulfhydryl SH groups, resulting in inhibiting SH-containing enzymes and production of reactive oxygen species such as superoxide ion, hydrogen peroxide, and hydroxyl radical (39, 41, 45-47, 101, 105, 139, 169, 170). In addition to forming strong bonds with SH and other groups like OH, NH2, and Cl in amino acids which interfere with basic enzymatic processes, toxic metals exert part of their toxic effects by replacing essential metals such as zinc at their sites in enzymes. An example of this is mercury's disabling of the metallothionein protein, which is necessary for the transport and detoxification of metals. Mercury inhibits sulfur ligands in MT and in the case of intestinal cell membranes inactivates MT that normally bind cuprous ions (125, 141), thus allowing buildup of copper to toxic levels in many and malfunction of the Zn/Cu SOD function. Another large study (114) found a high percentage of autistic and PDD children are especially susceptible to metals due to the improper functioning of their metallothionein detoxification process, and that with proper treatment most recover. Mercury has also been found to play a part in neuronal problems through blockage of the P-450 enzymatic process (141). Mercury induced reactive oxygen species and lipid peroxidation has been found to be a major factor in mercury's neurotoxicity, along with leading to decreased levels of glutathione peroxidation and superoxide dismustase (SOD) (39). This has been found to be a major factor in neurological and immune damage caused by the heavy metals, including damage to mitochondria and DNA (37-40, 170), as well as chronic autoimmune conditions and diseases (29) . Turmeric (curcumin) has strong antioxidant effects and has been shown to counteract lipid peroxidation and toxicity effects of metals and to reduce the toxic effects of metals such as copper, lead, cadmium, etc. (171).

The effects on DNA are a factor in several of the toxic metals such as arsenic, beryllium, cadmium, chromium, and nickel being known carcinogens (147), but chronic exposure to other toxic metals such as mercury are also known to promote cancer through their DNA effects and suppression of the immune system (170).

Metals by binding to SH radicals in proteins and other such groups can cause autoimmunity by modifying proteins which via T-cells activate B-cells that target the altered proteins inducing autoimmunity as well as causing aberrant MHC II expression on altered target cells (136). Studies have also found mercury and lead cause autoantibodies to neuronal proteins, neurofilaments, and myelin basic protein (137, 155, 45); and immune mechanisms are a major factor in neurotoxicity of metals seen in conditions such as autism and ADD (98b, 169).

Although vaccinations appear to be the largest source of mercury in infants, mercury has been found to be transmitted from the mother to the fetus through the placenta and accumulate in the fetus to higher levels than in the mother's blood (30, 169b). Breast milk of women who have amalgam fillings is the second largest source of mercury in infants and young children (169b, 69), but eating a lot of fish has also been found to be a significant source of methyl mercury (101). Milk increases the bioavailability and retention of mercury by as much as double (169b, 131, 31) and mercury is often stored in breast milk and the fetus at much higher levels than that in the mother's tissues (169b, 31). Mercury is transferred mainly by binding to casein (131, 92). The level of mercury in breast milk was found to be significantly correlated with the number of amalgam fillings (31, 169b), with milk from mothers with 7 or more fillings having levels in milk approx. 10 times that of amalgam-free mothers. The mercury in milk sampled ranged from 0.2 to 6.9 μg/L. Prenatal mercury exposure can also developmentally damage the metals detox system of the liver which can lead to accumulation and toxicity of later metals exposure (169b).

High lead, copper, manganese, or mercury levels have been found to be associated with attention deficit hyperactivity disorder (ADHD), memory deficits, impulsivity, anger, aggression, inability to inhibit inappropriate responding, juvenile delinquency, and criminality (19, 20a, 21, 61, 62, 83, 122, 133, 134, 145, 150-155, 159, 169). Mercury has been found to be a factor in anger, aggressive behavior, depression, obsessive compulsive behavior (OCD), ADD, autism, schizophrenia, suicidal behaviors, learning disabilities, anxiety, mood disorders, and memory problems (135, 133, 149, 150, 153-155, 157, 169, 170, 15, 113-115). It has been found that excess levels of copper can cause violent behavior in children (124, 115, 15, 114). A study that investigated the effects of zinc and copper on the behavior of schizophrenic patients by comparing blood zinc and copper levels in criminal and noncriminal schizophrenic patients found criminal subjects have significantly lower zinc levels and signif. higher copper levels than non-criminal subjects (165).

Manganese toxicity has long been known to be associated with impulsive and violent behavior (37, 61a, 134, 151). Lead also has been the subject of extensive research documenting its relation to all of these conditions (19-21, 61, etc.). Based on a national sample of children, there is a significant assoc. of lead body burden with aggressive behavior, crime, juvenile delinquency, behavioral problems (62b). By the government's latest count, 2.2 percent of children ages 1 to 5 in the United States - 300,000 children - have a blood lead level that is greater than or equal to 10 micrograms per deciliter of blood, a level that studies have shown to be associated with adverse effects. In a recent study after adjustment for covariates and interactions and removal of noninfluential covariates, adjudicated delinquents were four times more likely to have bone lead concentrations ¿25 ppm than controls (21a).

High aluminum levels have been found to be related to encephalopathies and dementia (49, 15). Scores for tension, depression, anger, fatigue and confusion in workers exposed to aluminum for more than ten years were significantly more than those in non-exposed controls (49). "Recent studies suggest that aluminum contributes to neurological disorders such as Alzheimer's disease, Parkinson's disease, senile and presenile dementia, clumsiness of movements, staggering when walking, and inability to pronounce words properly". Arsenic, like most of the other metals has been found in studies to be associated with neurologic, vascular, dermatologic, and carcinogenic effects, along with reproductive effects (100, 15c). Long-term exposure to ingested arsenic has been documented to induce peripheral vascular disease, cartoid arteriosclerosis, ischemic heart disease, and cerebral infarction in a dose-response relationship. A comparison of areas with higher levels of arsenic in the water supply found higher fetal and infant mortality in areas with higher arsenic levels and higher cancer rates. Cadmium is also a known carcinogen (100c, d). Some of the developmental effects documented to be caused by low level toxic metal exposure include developmental delays, growth problems, slower reaction times, diminished intellectual ability, behavior problems, poor balance and motor function, hearing loss, attention deficit disorder, etc. (19, 159, 169, 170, etc.)

Many individuals have been found to be more sensitive to toxic metals depending on genetic sensitivity and past exposure to toxic substances (28, 29). Nickel exposure is common and nickel exposure has been found to be significantly related to perinatal unthriftiness and mortality in animal studies. Large numbers of people affected by allergic conditions such as eczema and psoriasis vulgaris (59) and serious autoimmune conditions such as lupus and CFS have been found to be immune reactive to nickel or mercury (28, 29, 59, 43a, 170).

Other agents including mercury are known to accumulate in endocrine system organs such as the pituitary gland, thyroid, and hypothalamus and to alter hormone levels and endocrine system development during crucial periods of development (33, 37, 27, 109, 111, 155, 170). Such effects are usually permanent and affect the individual throughout their life. Pregnant women who suffer from hypothyroidism (underactive thyroid) have a four-times greater risk for miscarriage during the second trimester than those who don't, and women with untreated thyroid deficiency were four-times more likely to have a child with a developmental disabilities and lower IQ (111) . Some of the documented effects of exposure to toxic metals include significant learning and behavioral disabilities, mental retardation, autism, etc. But even some of the relatively subtle effects that have been found to occur such as small decreases in IQ, attention span, and connections to delinquency and violence, if they occur in relatively large numbers over a lifetime can have potentially serious consequences for individuals as well as for society (21, 26, 37, 41, 42, 113-115, 155).

The incidence of neurological conditions in children such as autism has increased over 500% in the last decade (80, 143, 149, 169), along with similar increases in ADD and other pervasive developmental diseases (PDD). Autism is a condition that was unknown prior to the 1940s but whose incidence has increased so rapidly that it is currently the 3rd leading childhood neurological conditions and the current incidence in approximately 1 in 300, and 1 in 150 in some communities surveyed in Maryland (80). Millions of kids are currently afflicted with PDD conditions. Mercury and other toxic metals have been found to be a factor in most of those tested (81, 99, 153, 169). Vaccinations that use mercury thimerosal as a preservative appear to be a common and causative factor in these conditions as well as SIDS (81, 83, 99, 122, 149, 169). A study at the U.S. CDC and followup studies found "statistically significant associations" between certain neurologic developmental disorders such as attention deficit disorder (ADD) and autism with exposure to mercury from thimerosal-containing vaccines before the age of 6 months (122, 149, 169).

The authors of a new study of thimerosal developmental effects (149b) write:

> "Our studies . . . provide evidence that mercury, heavy metals and the vaccine preservative thimerosal potently interfere with [methionine synthase] activation and impair folate-dependent methylation. Since each of these agents has been linked to developmental disorders, our findings suggest that impaired methylation, particularly impaired DNA methylation in response to growth factors, may be an important molecular mechanism leading to developmental disorders."

Citing Stajich et al 2002 (J Peds) and Pichichero et al 2002 (Lancet), Waly et al write:

> "A single thimerosal-containing vaccination produces acute ethylmercury blood levels of 10-30nM . . . , and blood samples in 2-month-old infants, obtained 3-20 days after vaccination, contain 3.8-20.6 nM ethylmercury . . . Our studies therefore indicate the potential for thimerosal to cause adverse effects on [methionine synthase] activity at concentrations well below the levels produced by individual thimerosal-containing vaccines."

A direct mechanism involving mercury's inhibition of cellular enzymatic processes by binding with the hydroxyl radical (SH) in amino acids appears to be a major part of the connection to these allergic/immune reactive conditions (81, 83, 89-91, 97, 105, 170). For example mercury has been found to strongly inhibit the activity of xanthine oxidase and dipeptyl peptidase (DPP IV) which are required in the digestion of the milk protein casein (89, 91, 93), and the same protein that is cluster differentiation antigen 26 (CD26) which helps T lymphocyte activation. CD26 or DPPIV is a cell surfact glycoprotein that is very susceptible to inactivation by mercury binding to its cysteinyl domain. Mercury and other toxic metals also inhibit binding of opioid receptor agonists to opioid receptors, while magnesium stimulates binding to opioid receptors (89). Studies involving a large sample of *autistic and schizophrenic patients*[3] found that over 90% of those tested had high levels of the milk protein beta-casomorphin-7 in their blood and urine and defective enzymatic processes for digesting milk protein (92, 93, 83), and similarly for the corresponding enzyme needed to digest wheat gluten (92, 94).The studies found high levels of Ig A antigen specific antibodies for casein, lactalbumin and beta-lactoglovulin and IgG and IgM for casein. Beta-casomorphine-7 is a morphine like compound that results in neural dysfunction (92), as well as being a direct histamine releaser in humans and inducing skin reactions (91c, 92). Similarly many also had a corresponding form of gluten protein (94). Elimination of milk and wheat products and sulfur foods from the diet has been found to improve the condition. A double blind study using a potent opiate antagonist, naltrexone (NAL), produced significant reduction in autistic symptomology among the 56% most responsive to opioid effects (95). The behavioral improvements was accompanied by alterations in the distribution of the major lymphocyte subsets, with a significant increase in the T-helper-inducers and a significant reduction of the T-cytotoxic-suppressors and a normalization of the CD4/CD8 ratio. Studies have found mercury causes increased levels of the CD8 T-cytotoxic-suppressors (96). As noted previously,

[3]**Internet:** "http://www.flcv.com/autismgc.html".

such populations of patients have also been found to have high levels of mercury and to recover after mercury detox (29, 81, 83, 99, 170). As mercury levels are reduced, the protein binding is reduced and improvement in the enzymatic process occurs (29, 83, 170).

Additional cellular level enzymatic effects of mercury's binding with proteins include blockage of sulfur oxidation processes and neurotransmitter amino acids which have been found to be significant factors in many autistics (90, 97, 105, 83), plus enzymatic processes involving vitamins B6 and B12, with effects on the cytochrome-C energy processes as well.

The activating enzyme B6-kinase is totally inhibited in the intestine at extremely low levels (nanamolar) of mercury (121), with similar effects on B12. Epson salts (magnesium sulfate) baths, supplementation with the p5p form of Vit B6 and vit B12 shots are methods of dealing with these enzymatic blockages that have been found effective by those treating such conditions. Vit B complex and Vit E ammeliorate methyl mercury effects (158). Mercury and toxic metals have also been found to have adverse effects on cellular mineral levels of calcium, magnesium, zinc, and lithium (46, 170, 83, 154). Supplementing with these minerals has also been found to be effective in the majority of cases (46, 68-70) Another of the results of these toxic exposures and enzymatic blockages is the effect on the liver and dysfunction of the liver detoxification processes which autistic children have been found to have (81, 97, 169). All of the autistic cases tested were found to have high toxic exposures/effects and liver detoxification profiles outside of normal (81c, 169).

According to studies reviewed, over 20% of the children in the U.S. have had their health or learning significantly adversely affected by toxic metals such as mercury, lead, and cadmium; and over 50% of children in some urban areas have been adversely affected. Significant behavioral effects were also documented. Such effects similarly affect adults (37, 170). Many epidemiologist believe the evidence demonstrates that over 50% of all U.S. children have had their learning ability or mental state significantly adversely affected by prenatal and/or postnatal exposure to toxic substances (1, 2, 32c, 87, 108, etc.). The toxic metals have been documented to be reproductive and developmental toxins, causing birth defects and damaging fetal development, as well as neurological effects, developmental delays, learning disabilities, depression, and behavioral abnormalities in many otherwise normal-appearing children (5-33, 37-42, 48, 66, 83, 84, 112-115, 151-155, 169).

Prenatal exposure to 7 heavy metals was measured in a population of pregnant women at approximately 17 weeks gestation (9). Follow-up tests on the infants at 3 years of age found that the combined prenatal toxic exposure score was negatively related to performance on the McCarthy Scales of Children's Abilities and positively related to the number of childhood illnesses reported. Many similar studies measuring child hair levels of the toxic metals aluminum, arsenic, cadmium, lead, and mercury have found that these toxic metals have significant effects on learning ability and cognitive performance, explaining as much as 20% of cognitive differences among randomly tested children who have low levels of exposure not exceeding health guidelines for exposure to any of these metals (6-15, 17, 19). These toxic metals have been found to have synergistic negative effects on childhood development and cognitive ability (8, 13-15, 66).

Among those more significantly affected by neurological deficits or problems, the affects appear even more significant. Comparison of groups of children who are mentally retarded or significantly learning disabled to normal controls found significantly higher levels of toxic metals in the affected groups (7, 11, 17, 18, 21), with the level of the toxic metals and minerals known to be affected by them correctly identifying those with significant disabilities in from 90 to 98% of cases in the studies. A study of rural children with subtoxic exposure levels found significantly higher levels of lead and cadmium in a group of mildly retarded/borderline intelligence (IQ 55-84) than controls (11). 76% of the study group had one of 5 toxic metals exceeding the lab's upper safety limit.

A large study found that hair cadmium level is highly correlated with and predictive of very significant learning disability or mental retardation (18). Over 90% of those with hair cadmium levels of 0.4 parts per million or more were found to have significant disabilities and over 95% of those with levels above 0.7 were mentally retarded. In a group of students with normal range IQs who failed one subject area on a standardized test (paradigmatic LD), the groups cadmium and lead hair levels were significantly higher than controls; and hair metal levels with lithium levels included correctly separated the groups with 95% accuracy (7). Average hair cadmium levels in the group with learning disabilities was 1.7 ppm. Similar findings regarding toxic metal exposure levels were found for dyslexic children (10), schizophrenic children (16, 157), and autistic children (16). A study of dyslexic children with normal IQs found the dyslexic group had a cadmium hair level average of 2.6 ppm, 25 times that of the control group (10) and exceeding the maximum of the normal acceptable range. The dyslexic group also had somewhat higher aluminum and copper levels. Studies of groups with schizophrenia have found increased levels of copper and mercury and reduced levels of zinc, magnesium and calcium, which are known to be inhibited by heavy metals and affect neurotransmitter levels (113, 49). Results of a study at a teaching hospital showed that cadmium was significantly raised in depressives and reduced in mania patients. Lead was increased in depressives and schizophrenics but not in mania patients. Serum zinc was reduced in all mental patients (164). A group of violent criminals had signif. higher levels of hair lead and cadmium levels than non violent controls (62b).

These toxic metals have also been found similarly to have significant behavioral and emotional effects on children and adults (6-8, 11, 14-16, 19, 21, 83, 169, 170). One group of students were scored by their classroom teacher on the Walker Problem Behavior Identification Checklist (WPBIC). A combined hair level score for mercury, lead, arsenic, cadmium and aluminum was found to be significantly related to increased scores on the WPBIC subscales measuring acting-out, disturbed peer relations, immaturity, and the total score (6) among a population of students with no known acute exposures. The combined metals score explained 23% of the difference of the total WPBIC score, and 16 to 29% of the differences on the subscales for withdrawal, acting out, disturbed peer relations, distractibility, and immaturity (6). Similar results were found in the other studies, and have been found to have implications not only in the classroom but on relations at home, on driving habits, and on job performance.

Studies have found evidence that abnormal metal and trace elements affected by metal exposure appear to be a factor associated with aggressive or violent behavior (37, 48, 60-63, 110, 115, 21), and that hair trace metal analyses may be a useful tool for identifying those prone to such behavior. It has been found that excess levels of copper can cause violent behavior in children (124, 115). One mechanism found to be associated with toxic metals and pesticides relation to aggressive and violent behavior is the documented inhibition of cholinesterase activity in the brain (110). Another series of studies found abnormal trace metal concentrations to be associated with violent-prone individuals including elevated serum copper and depressed plasma zinc (115, 161). A group with a history of assaultive and violent-prone behavior had significantly higher median Cu/Zn ratio than for controls. Assaultive, violent-prone individuals usually have abnormal trace-metal concentrations, including elevated serum copper and depressed plasma zinc (115b).

A study of teenagers in Pittsburgh found that having elevated lead was associated with a four-fold risk of delinquency (21). Similar tests in the California juvenile justice system as well as other studies have found significant relations to classroom achievement, juvenile delinquency, and criminality (62, 63, 120). Three studies in the California prison system found those in prison for violent activity had significantly higher levels of hair manganese than controls (61, 37, 115a), while other studies in the California prison and juvenile justice systems found that those with 5 or more essential mineral imbalances were 90% more likely to be violent 50% more likely to be violent for 2 or more mineral imbalances (120). In studies at juvenile delinquency centers, nutritional therapy reduced antisocial and violent behavior by over 50% (120, 115).

A study analyzing hair of 28 mass murderers found that all had high metals and abnormal essential mineral levels (115). Like several other studies they found higher levels of such toxic metals in blacks than in Caucasian populations. Studies of an area in Australia with much higher levels of violence as well as autopsies of several mass murderers also found high levels of manganese to be a common factor (37, 115a). Such violent behavior has long been known in those with high manganese exposure. Doctors in UK found a woman's insanity and violent behavior to be related to poisoning from leaking amalgam dental fillings (37), and other studies and clinical results have confirmed the connection of toxic metals to behavioral problems and violence (113c, 115, 119, 120). Studies at the Argonne National Laboratory found that the majority of delinquents and criminals had high metals levels such as cadmium and lead, and to fall into 2 categories. One group with high copper and low zinc, sodium potassium tended to have extreme tempers, while another group with low zinc and copper, but high sodium and potassium tended to be sociopathic (115). But it was found that treatment of delinquent or violent prone individuals for metals related problems including nutritional therapy usually produced significant improvements in mood, violent behavior, and functionality - with complete cure in the majority of cases (115, 119, 120).

Lithium protects brain cells against excess glutamate and calcium, and low levels cause abnormal brain cell balance and neurological disturbances (75, 79). Lithium also is important in Vit-B12 transport and distribution, and studies have found low lithium levels common in learning disabled children, incarcerated violent criminals, and people with heart disease (76, 78).

Lithium supplementation has been found to be an effective treatment adjunct in conditions such as bipolar depression, autism, and schizophrenia where mania or extreme hyperactivity are seen (104, 79). It has been documented that conditions like depression and other chronic neurological conditions often involve damage and nerve cell death in areas of the brain like the hippocampus, and lithium has been found to not only prevent such damage but also promote cell gray matter cell growth in such areas (79), and to be effective in treating not only depressive conditions but degenerative conditions like Huntington's Disease which are related to such damage.

Lithium had a significant mood-improving and stabilizing effect on former drug users with psychological conditions (77). In the study a group including violent offenders and family abusers were divided into 2 groups. Half got lithium supplements and half a placebo. The group getting lithium had significantly increased scores for mood, happiness, friendliness, and energy, while the other group did not (77). Similar results were obtained for a group of violent former drug users. In a large Texas study, incidence of suicide, homicide, rape, robbery, burglary, theft, and drug use were significantly higher in counties with low lithium levels in drinking water (78). In a placebo controlled study on prisoners with a history of impulsive/aggressive behavior, the group taking lithium supplements had a significant reduction in aggressive behavior and infractions involving violence (78). The authors suggest that for those areas with low lithium levels in water, water systems should add lithium; and those with deficiencies in lithium or displaying aggressive or impulsive behavior would likely benefit from lithium supplements (78).

Toxic metals and the resulting mineral imbalances have also been found to be a major cause of depression and mood disorders including schizophrenia and mania (43, 48, 69, 70, 83, 84, 112-114, 157, 19, 21, 66, 169). Some factors that have been documented in depression, impulsiveness, and violent behavior are low serotonin levels, abnormal glucose tolerance (hypoglycemia), and low chromium and folate levels (126-130, 113, 115), which mercury has also been found to be a cause of. One mechanism by which mercury has been found to be a factor in aggressiveness and violence is its documented inhibition of the brain neurotransmitter acetylcholinesterase (5, 19, 28, 44-47, 83, 110, 170). Low serotonin levels and/or hypoglycemia have also been found in the majority of those with impulsive and violent behavior (127, 128, 115). Toxic metals also influence mood and depression by affecting balances of essential minerals and essential fatty acids, along with blocking essential enzymatic processes resulting in morphine like substances in the blood, and affecting levels of most brain neurotransmitters. Another well documented mechanism of toxic metal depression inducement is through reducing amino acid levels such as tryptophan and tyrosine which is documented to result in inducing depression (83, 85, 86, 66), while another is mercury's promotion of candida albicans overgrowth (112) . Mercury and lead have been documented to be causes of autism, schizophrenia, mania, ADD, and depression (48, 81, 83, 48, 149, 23, 169, 113, 19, 66), while vanadium has been found to be a cause of depressive psychosis and mania (84). Mercury accumulates in the pituitary gland (170, 109) and thus has endocrine system/hormonal effects. In addition to mercury having estrogenic effects (33, 37, 170) mercury and lead have other documented hormonal effects (111, 109, 155, 170), including lowered levels of neurotransmitters dopamine, serotonin, and noreprenephrine (66, 139, 170). Some of the effect on depression is also related to mercury's effect of reducing the level of posterior pituitary hormone (oxytocin). Low levels of pituitary function are associated with depression and suicidal thoughts, and appear to be a major factor in suicide of teenagers and other vulnerable groups. Amalgam fillings, nickel and gold crowns are major factors in reducing pituitary function (109, 170). Supplementary oxytocin extract has been found to alleviate many of these mood problems (35), along with replacement of metals in the mouth (109, 170). A study following infants to age 7 in New Zealand found a significant effect on cognitive and psychological function related to mother's hair mercury level (146). A study of children in the Faeroe Islands had a similar finding (146b).

Other endocrine effects of mercury and lead include infertility and other reproductive system problems (33, 35, 170, 148)

Studies have previously found that low levels of lead exposure is significantly related to hyperactivity and attention deficit (19, 20a, 21, 83, 114b, 159), depression (48, 113b), school cognitive performance (19, 20a, 22, 23, 50, 60a, 159), behavioral problems (19, 21, 22, 23, 48, 115), mental disorders (24, 48, 115), allergies (60), growth (54), gestational age (54), and spontaneous abortions (60). In one study children's umbilical cord blood at birth was recorded and a teacher assessment of learning/behavioral characteristics completed at the end of the school year at age 8 (20a). Girls with higher than average (¿ 10 μg/dL) chord blood level were found to be more likely to be dependent, inpersistant, and have an inflexible approach to tasks. (10 μg/dL blood approx. 8 ppm hair, #52) Boys with higher than average chord blood level were found to be more likely to have problems following simple directions or sequences of directions. A follow up study to the Cincinnati lead study measured blood lead levels and compared to standardized IQ test scores at approximately 6.5 years of age (50). The study found blood lead levels were significantly inversely related to both full-scale and performance IQ, and that blood lead levels over 20 μg/dL were related to an average deficit in IQ of 7 points on performance IQ as compared to those with below 10 μg/dL blood lead levels. Another study in Australia measured IQ at approximately 12 years of age and compared to blood lead levels measured from 1 to 7 years of age (51). Total, verbal, and performance IQ were all significantly inversely related with blood lead levels measured during the first 7 years of life. Two studies found average hair lead levels in groups of learning disabled children over 20 ppm (7, 12), compared to 4 ppm in controls.

But the author of a recent study (23) states that "There is no safe level of blood lead". Children with a lead concentration of 7 to 10 micrograms per deciliter of blood scored an average of 11.1 points lower than the mean on the Stanford-Binet IQ test, the researchers found. The study also found an average 5.5-point decline in IQ for every additional 10-microgram increase in blood-lead concentration, said Dr. Lanphear. Another study found significant IQ reductions approx. 0.74 points per μg/dL lead level increase at exposure levels between 1 μg/L and 10 μg/dL (23b).

However other studies have pointed out that these studies generally did not investigate or consider the effects and synergistic interactions of the other toxic metals (6, 11, 20, 28), and the fact that lead and cadmium levels tend to have positive correlations with each other. A study of rural school children without acute exposures and with IQS in the normal range found highly significant relations between lead and cadmium with intelligence scores and school achievement tests (12). Lead and cadmium explained 29% of the variance in IQ. These two metals have been found to have different mechanisms of CNS damage, with cadmium affecting verbal ability more and lead affecting performance measures more. The author of another study (28) of 9 year olds living in an area near an incinerator in Ohio concluded that part of the developmental effects attributed to lead in many past studies was mostly due to cadmium effects, with lead serving as a marker for cadmium effects due to their common origins and cadmium's effect of increasing lead accumulation. The findings of this study were generally consistent with a previous study (12) regarding higher levels of cadmium and lower levels of zinc in children with cognitive deficits. However this study found zinc level, though significantly affected, can be increased in some depending on other factors. Cadmium as previously noted as well as mercury have anti metabolite effects that significantly affect calcium, zinc, and phosphate levels in the body (74, 28, 170). The reduction in zinc levels causes increased absorption of lead, and cadmium's affect on the pyrimidine-5-nucleotidase enzyme inhibits phosphorylation in the energy/respiratory ATP function (28). This study found the level of hair phosphorous, as affected by cadmium exposure, was the best indicator of cognitive function and dysfunction. Lead was found to have a lesser effect on phosphorous level and ATP function. The entire group of learning disabled boys had low hair phosphorous levels compared to those without learning disabilities. The main factors appearing to affect those with high cadmium levels and low phosphorous hair levels were living within 2 miles of the incinerator, exposure to passive cigarette smoke, and living in a rural area that may have had high cadmium levels in wells. Another study found heavy smokers have cadmium levels in body tissues about 2 times that of non smokers, and hair cadmium levels in newborns of smokers were twice as great as in newborns of non smokers (53).

Other studies have found that cadmium causes significant decreases in birth weight through its antimetabolite actions (53, 54) and significant increases in blood pressure (55). Newborn hair cadmium levels have been found to be significantly correlated to maternal hair levels and mothers exposed occupationally to heavy metals to have hair levels twice as high as controls (54). Likewise adults with higher than average cadmium levels performed less well on measures of attention, psychomotor speed, and memory (56).

These toxic metals have also been found to have significant effects on motor-visual ability and performance (6a, 8, 19, 20, 170), as measured by the Bender Visual-Motor Gestalt Test score. Arsenic, lead, and cadmium levels had the highest correlation with cognitive scores, while aluminum had a significant relation mostly with motor-visual performance and mercury had lesser but highly significant correlations to both.

Studies have also found evidence of a connection between low levels of zinc and four other common childhood diseases, treatment resistant depression (70), oppositional defiant disorder (161), childhood-onset *diabetes*[4] (72) and *epilepsy*[5] (73). Zinc is an antagonist to toxic metals like cadmium and mercury, and adequate levels are required to balance the adverse effects of these toxic metals on cellular calcium and other enzymatic processes (28, 74). Other connections between mercury and type1 diabetes have also been demonstrated. Mercury has been found to cause an increase in inflammatory Th2 cytokines (116). In the pancreas, the cells responsible for insulin production can be damaged or destroyed by the chronic high levels of cytokines, with the potential of inducing type II diabetes - even in otherwise healthy individuals with no other risk factors for diabetes (117). Mercury inhibits production of insulin and is a factor in diabetes and hypoglycemia, with significant reductions in insulin need after replacement of amalgam filings and normalizing of blood sugar (109). A connection between mercury in vaccines and *epilepsy*[6] has also been found (118).

It should be noted that both blood and hair mercury level have been found to not be highly correlated to exposure from mercury vapor, which is the most common exposure from mercury, because of special properties of mercury (170). Mercury vapor has an extremely short half life in blood, and rapidly crosses cell membranes in body organs where it is oxidized to inorganic mercury, accumulating in the brain, heart, kidneys, and other locations. Thus although elemental mercury exposures are typically greater than organic exposures, most mercury in the blood is organic. Likewise

[4]**Internet:** "http://www.home.earthlink.net/%7Eberniew1/diabetes.html".
[5]**Internet:** "http://www.home.earthlink.net/%7Eberniew1/epilepsy.html".
[6]**Internet:** "http://www.home.earthlink.net/%7Eberniew1/diabetes.html".

hair mercury has been shown to be more highly correlated with organic mercury exposure than with inorganic (170). Hair test are affected by external mercury exposure in occupational exposures such as dental offices which typically have fairly high levels of mercury. Other measures of mercury such as stool, saliva, and urine have been found to be better measures of mercury for such cases. Urine contains mostly inorganic mercury, but becomes less reliable with long term chronic exposure due to cumulative damage to the urinary detox system. Urinary fractionated porphyrin test is a good test of metabolic damage that has occurred due to mercury of other toxics. The level and distribution of the 6 porphyrins measured indicates extent of damage as well as likely source of damage (170).

Hair levels have been found to be generally reliable indicators of recent environmental metal exposures other than mercury (28, 52, 54, 58), and to be better correlated with symptoms than blood test (88). Similarly, blood levels have been found to not reflect chronic or historic cadmium exposure (52, 53, 58) since metals such as cadmium and mercury have extremely short half life in the blood but long half life in the body. Air measurements of cadmium or mercury tend to be very unreliable due to the small particle size, dispersion variation, and other factors. Measure of accumulation in area plants is one reasonably reliable method; areas with cadmium levels over 0.5 ppm indicate significant air pollution.

Manganese can downregulate serotonin function, reducing sociability and increasing aggressiveness or depression. Excess manganese exposure reduces dopamine levels which can result in violent behavior. Higher levels of manganese exposure are correlated with Parkinson's Disease and violent behavior (151). The most common significant source of high manganese neonatal exposure is from soy infant formulas, which typically have very high levels of manganese (151, 156).

Because lead and other toxic metals are retained in bone and astroglial cells in the brain, uptake during fetal development and early childhood has long-lasting effects on development and behavior (151). Among the toxic effects of lead is a reduction of dopamine function (which disturbs the behavioral inhibition mechanisms in the basal ganglia) and glutamate (which plays an essential role in the long term learning associated with the hippocampus). Research at the individual level showed that the uptake of heavy metals is associated with higher levels of learning disabilities, hyperactivity, substance abuse, violent crime, and other forms of anti-social behavior. In seven different samples of prison inmates, violent offenders had significantly higher levels of lead, cadmium, or manganese in head hair than non-violent offenders or controls. In two prospective studies, high lead levels at age 7 (one measuring lead in blood, the other bone lead) predicted juvenile delinquency and adult crime. A substantial proportion of individuals diagnosed with ADD/ADHD are likely to have dangerously high levels of lead, manganese, or cadmium in bodily tissues. Children with blood lead levels of more than 2 micrograms per deciliter were four times more likely to have ADHD than children with levels below 0.8 microgram per deciliter (167). Because alcohol, cocaine and other drugs temporarily restore neurotransmitter functions that are abnormal, substance abuse may often be crude self-medication in response to the effects of toxicity. For example, because lead downregulates dopamine and cocaine is a non-selective dopamine reuptake inhibitor, lead toxicity could increase the risk of cocaine abuse (151).

Heavy metals compromise normal brain development and neurotransmitter function, leading to long-term deficits in learning and social behavior (151). At the individual level, earlier studies revealed that hyperactive children and criminal offenders have significantly elevated levels of lead, manganese, or cadmium compared to controls; high blood lead at age seven predicts juvenile delinquency and adult crime. At the environmental level, our research has found that environmental factors associated with toxicity are correlated with higher rates of anti-social behavior. For the period 1977 to 1997, levels of violent crime and teenage homicide were significantly correlated with the probability of prenatal and infant exposure to leaded gasoline years earlier. Across all U.S. counties for both 1985 and 1991, industrial releases of heavy metals were – controlling for over 20 socio-economic and demographic factors – also a risk-factor for higher rates of crime. Excess levels of lead and manganese are correlated with ADHD and violent behavior. Poor diet increases the effects of lead and manganese toxicity. Communities with a higher percentage of children having blood lead over 10 mg/dL are significantly more likely to have higher rates of violent crime and higher rates of educational failure. Studies comparing Toxic Release Inventory (TRI) data to crime rate data for all U.S. counties found a positive correlation between releases of lead and manganese and violent crime rates. Specialists at the Pfeiffer Treatment Center in Illinois have found that treatments to reduce levels of lead and other toxins provide lasting improvement without medication (151).

Surveys of children's blood lead in Massachusetts, New York, and other states as well as NHANES III and an NIJ study of 24 cities point to another environmental factor: where silicofluorides are used as water treatment agents, risk-ratios for blood lead over 10μg/dL are from 1.25 to 2.5, with significant interactions between the silicofluorides and other factors associated with lead uptake (152). Communities using silicofluorides also report higher rates of learning disabilities, ADHD, violent crime, and criminals who were using cocaine at the time of arrest.The use of fluosilicic acid (H2SiF6) to fluoridate public water supplies significantly increases the amounts of lead in the water (whereas the use of sodium silicofluoride (NaSiF6) or sodium fluoride (NaF) does not. Communities using either fluosilicic acid (H2SiF6) or sodium silicofluoride (NaSiF6) have significantly higher rates of crime than those using sodium fluoride or delivering unfluoridated water. Also where silicofluorides are in use, criminals are more likely to consume alcohol, more likely to have used cocaine at time of arrest - and that communities have significantly higher crime rates. For 105 New York communities, for every age and racial group there was a significant association between silicofluoride treated community water and elevated blood lead. Data from analysis of national sample of over 4,000 children in NHANES III, show that water fluoridation is associated with a significant increase in children's blood lead (with especially strong effects among minority children). (152)

1.4 Sources of exposure to toxic metals

The studies reviewed suggest that exposure to toxic metals may account for over 20% of learning disabilities, 20% of all strokes and heart attacks, and in some areas be a factor in over 40% of all birth defects (87, 169, 169, 170, etc.). The U.S. Center for Disease Control has found that primary exposure to lead is from soil, paint chips, drinking water, fertilizer, food, auto and industrial emissions, ammunition (shot and bullets), bathtubs (cast iron, porcelain, steel), batteries, canned foods, ceramics, chemical fertilizers, cosmetics, dolomite, dust, foods grown around industrial areas, gasoline, hair dyes and rinses, leaded glass, newsprint and colored advertisements, paints, pesticides, pewter, pottery, rubber toys, soft coal, soil, solder, baby formula using tap water, tobacco smoke, vinyl 'mini-blinds', and dust (35, 108). High levels of cadmium are found in regions with high emissions from incinerators, coal plants, or cars (28), as well as in shellfish (36), art supplies, bone meal and cigarette smoke (28). Other common sources include rural drinking water wells (28, 35), processed food, fertilizer, and old paint, food (coffee, fruits, grains, and vegetables grown in cadmium-laden soil, meats [kidneys, liver, poultry], or refined foods), freshwater fish, fungicides, highway dusts, incinerators, mining, nickel-cadmium batteries, oxide dusts, paints, phosphate fertilizers, power plants, seafood (crab, flounder, mussels, oysters, scallops), sewage and industrial sludge spread on farmland (142), "softened" water, smelting plants, tobacco and tobacco smoke, and welding fumes. Since the half-life of lead in the blood is only 25 days, blood tests are not a reliable test for lead body burden (25c). Hair element test is another option (19).

Common exposures to aluminum include aluminum cookware, antiperspirants, antacids, processed cheese and other processed food, lipstick, medications and drugs (anti-diarrheal agents, hemorrhoid medications, vaginal douches), "softened" water, and tap water. Common sources of arsenic include antibiotics given to commercial livestock, air pollution, chemical processing, coal-fired power plants, defoliants, drinking water, drying agents for cotton, fish and shellfish, herbicides, insecticides, meats (from commercially raised poultry and cattle), metal ore smelting, pesticides, seafood (fish, mussels, oysters), specialty glass, and wood preservatives. Nickel, which is highly toxic and commonly causes immune reactions, is commonly seen in dental crowns and braces, along with jewelry, etc. (nickel and inorganic mercury commonly produce allergic type autoimmune problems, 29). Manganese and other metal exposure can come through welding or metal work as well as from soy milk and soy products (151, 156). Cadmium, mercury, arsenic, chromium, silver, copper, and are other metals to which Floridians and others are commonly exposed in drinking water, food, or dental materials (34-36). Some of the toxic metals in food comes from land spreading of sewage and industrial waste on farmland (142).

The most common significant exposure for most people is to mercury vapor from amalgam fillings (43b). Most people with several amalgam fillings have daily exposure exceeding the U.S. government health guideline for mercury (4, 43b). Likewise a major exposure source of infants and young children is from placental transfer from their mother's amalgam fillings and breast feeding (43, 101, 107). The average amalgam filling has more than $^1/_2$ gram of mercury, and has been documented to continuously leak mercury into the body of those with amalgam fillings due to the low mercury vapor pressure and galvanic current induced by mixed metals in the mouth. Because of the extreme toxicity of mercury, only $^1/_2$ gram is required to contaminate the ecosystem and fish of a 10 acre lake to the extent that a health warning would be issued by the government to *not eat the fish*[7] [43]. Over 50,000 such warnings for 30% of U.S. lakes (1) and 10% of all U.S. river miles. All Great Lakes as well as many coastal bays and estuaries and large numbers of salt water fish carry similar health warnings.

Mercury is one of the most toxic substances commonly encountered, and according to Government agencies causes adverse health effects in large numbers of people in the U.S.[1, 2, 170] Based on widespread tests, the U.S. CDC estimates that approx. 10% of women of childbearing age, 6 million women, have current mercury levels that would put fetuses at risk of developmental neurological problems (1), without considering other common sources of mercury in infants. The extreme toxicity of mercury can be seen from documented effects on wildlife by very low levels of mercury exposure. The amount of mercury in the marine environment is increasing 4.8% per year, doubling every 16 years (1). Some Florida panthers that eat birds and animals that eat fish containing very low levels of mercury (about 1 part per million) have died from chronic mercury *poisoning*[8] (43). Since mercury is an estrogenic chemical and reproductive toxin, the majority of the rest cannot reproduce. The average male Florida panther has higher estrogen levels than females, due to the estrogenic properties of mercury. Similar is true of some other animals at the top of the food chain like polar bears, beluga and orca whales, and alligators, which are affected by mercury and other hormone disrupting chemicals.

Another major exposure source to infants is from thimerosal used in vaccinations as a preservative. The majority of infants get exposure above Government health guidelines for mercury and large numbers of infants with related neurological problems such as autism and ADD have been documented (81, 149). A major source of phenyl mercury is from mercury in paint, where many have been exposed to dangerous levels (106). The major source of exposure to organic (methyl) mercury is from fish and shellfish, but inorganic mercury has also been found to be methylated in the body by bacteria, yeast, etc. (43b). Significant levels of various forms of organic mercury have also been documented from dental work such as root canals and gold crowns over amalgam base (170, 29). Methyl mercury has been documented to be among the most potent developmental neurotoxicants (66, 101, 107), with evidence over 63,000 children are born each year with neurodevelopmental impairment due to prenatal exposure. Mercury vapor is the form that most readily crosses cellular membranes including the blood-brain barrier and placenta of pregnant women, and results in the highest levels in the major organs such as the brain, heart, and kidneys for a given level of exposure. But the average half-life of vapor in the blood is only seconds so blood tests are not a good measure of such exposure. For similar reasons hair mercury is a less accurate measure of body inorganic mercury burden than for the other metals. Both mercury vapor and organic mercury have been found to

[7] **Internet:** "http://www.flcv.com/damspr2f.html".
[8] **Internet:** "http://www.flcv.com/damspr2f.html".

be highly toxic and to have independent and synergistic effects at very low levels (170, 101, 107). However developmental effects have been found at comparable or lower levels from mercury vapor than from organic or inorganic exposure (170), and it has been well established that the primary exposure for most people is from mercury vapor from dental amalgam (43b).

1.5 Measures to reduce or alleviate toxic metal toxicity and behavioral problems

The most important measure to alleviate effects of toxic metals is avoidance of exposure or reducing current exposures. Significant improvement is usually seen after correcting digestive problems, eliminating allergens and environmental toxins, and improving nutrition (172, 173). Treatment centers around the following goals: improvement of GI function, restoration of normal immune function, elimination of heavy metals and other toxins, and supplementation to optimize hepatic, immunologic, neurologic, and cognitive function.

Chelation is the most effective component of treatment, showing significant improvement in most patients (173, 175) Chelators such as DMSA are often used (173) or spirulina or chlorella based products (172). This is supported by selenium, milk thistle (silimarin), NAC (starting with low dose of 25 mg/day increasing to 200 mg/day), calcium-D-glucarate, Alpha-ketoglutarate (for those with high ammonia), taurine (100 mg to 1000 mg), methionine (100 to 400 mg), plant based enzymes, GC free diet, omega-3 EFAs, probiotics, vit A, C, E, beta carotene, B complex and magnesium, zinc and multiminerals. Also pycogenol, L-theanine for calming effect and CoQ10, L-carnatine, L-carnosine, and DMAE for improved cognitive function (172, 173). Iron deficiency can also be a factor in ADHD (172).

Blood hypercoagulation has been found to be a factor in some cases of adult ADHD, with herbs such as curcumin, ginger, and ginkgo biloba found to be beneficial in treatment (172, 176). Structural studies show that some children with ADHD have decreased blood flow and energy use in the prefrontal cortex and striatum, which can also result in a decrease in brain volume of certain brain areas such as the areas related to attention. There can also be left hemispheric white matter deficits due to demyyelination and gray matter deficits in the right hemisphere. The drug Ritalin has been found to have an effect similar to the herbs discussed here in increasing regional cerebral brain flow in these areas (172), but unlike the herbs Ritalin has also been found to commonly have long term adverse health effects (145).

Current exposure levels of most common metals can be tested by a stool test kit from a lab such as Doctors Data Lab or Genova Diagnostic Lab, and recent exposures can be tested somewhat easier and cheaper by hair tests (see 66). Research information on common causes of chronic conditions and treatment information can be found on the Genova Diagnostic Lab web site (66).

As noted previously, most infants prior to 2003 got exposure to mercury beyond the federal government health guideline from mercury thimerosal used as a preservative in vaccinations (81). Since all vaccinations are now available mercury free, parents should request the mercury free version. Significant levels are also received through placental transfer and breast feeding by *mothers exposed to mercury through amalgam dental fillings*[9] or eating fish (30-32, 169b). Children with amalgam fillings get significant mercury exposure daily from their fillings (169b), and replacement reduces daily exposure level approximately 90% (43b).

Over 70% of mercury in the blood is commonly organic mercury, while the majority in the kidneys and urine is inorganic. The majority of exposure from amalgam is to vapor which rapidly is transmitted to cells throughout the body in blood and transformed to inorganic mercury in cells. There

[9] **Informativo:** "Infertility, Birth Defects, and Fetal Developmental Effects Related to Mercury from Amalgam Dental Fillings & Other Toxins".

is common conversion in the body between organic and inorganic mercury through methylation and demethylation processes (170, 43b), so type of mercury in the body does not indicate the original source of mercury.

For children with developmental or neurological conditions, a hair test can be used to assess toxic metal body burden (note that toxic metals affect cellular mineral levels so a large number of mineral level abnormalities can indicate toxicity effects, hair mercury level measures primarily organic mercury, virtually all with amalgam fillings have high mercury body burden). A urine fractionated porphyrin test can be used to assess metabolic effects. High levels of metals can be reduced by avoidance, replacement of metal dental work, use of mineral antagonists, oral chelators, and chemical chelation (66, 170, 172, 173).

Likewise, the majority of those with amalgam fillings have significant daily exposures often exceeding government health standards for mercury (43b) Daily inorganic mercury exposure can be assessed by stool or saliva test or mouth oral air measurement, but since many have been tested, several studies have developed analytical equations to estimate daily exposure based on number of amalgam surfaces in the mouth, which give reasonable estimates. The main way to reduce mercury exposure to elemental mercury is to avoid amalgam fillings and/or replace amalgam fillings by other materials. Other materials are available that perform as well as amalgam.

Seafood and fish[10] have often been found to have high levels of organic mercury, cadmium, and arsenic. For those eating significant amounts of such, the levels in the diet can be monitored by direct food testing or stool test for current exposure levels, or by hair or blood test. Fish and seafood from areas known to contain high levels of toxic metals should be eaten only occasionally if at all, depending on levels. Those who eat a lot of freshwater fish or seafood often have levels of mercury or some other metal exceeding government guidelines. Hair tests offer a reasonable reliable low cost method of assessing the level of many toxic metals in one test. In a large national survey, over 22% of those tested had *dangerous levels of mercury*[11]. Aluminum exposures can be reduced by avoiding aluminum antiperspirants, food cooked in aluminum cookware, and foods such as processed cheese that have high levels of aluminum.

As previously noted one of the main mechanisms of toxic effects is generation of free radicals and oxidative damage (66). This can be partially alleviated by eating foods high in antioxidants or supplementation of Vit A, C, E, along with such as grapeseed extract, pinebark extract, bilberry, etc. Bioflavinoids like bilberry and other fruits have been found to improve the function of the blood brain barrier. Vit C provides protection against toxicity of inorganic mercury by reducing the more toxic $Hg2+$ form to the less toxic $Hg+$ form of mercury. Vit B complex is also important to alleviate neurological effects. Most toxic metals also have mineral antagonist known to counteract toxic effects. For example selenium and zinc are antagonists of mercury, while zinc and iron are antagonists of cadmium (5, 64, 65, 74, 123). Iron (162) and zinc deficiencies, which can be caused by exposure to toxic metals, increase metal toxicities and supplementation can reduce toxicities, but they can also be toxic if levels are too high. Likewise calcium and magnesium deficiencies and imbalances have been seen to be caused by toxic metals, and proper supplementation can reduce toxicities and reverse conditions caused by these deficiencies or imbalances. Several studies have found that most children with ADHD have deficiencies of certain minerals that are commonly depleted by exposure to toxic metals, such as magnesium and zinc, and most show significant improvement after supplementation with these minerals (67-71, 83, 88, 163). Magnesium is the most common significant mineral deficiency among ADHD children (67-69, 172), but zinc is commonly deficient among children with ADHD and disruptive behavior disorder (68, 83, 19). Studies have found the level of free fatty acids also significantly lower in children with ADHD (70, 83, 19, 172), and some practitioners recommend supplementation of essential fatty acids as well in treatment of ADHD (172).

[10]**Internet:** "http://www.flcv.com/fishhg.html".
[11]**Internet:** "http://www.flcv.com/fishhg.html".

Large studies in schools in New York have found that dietary improvements and supplementation leads to large improvements in cognitive scores and large reductions in learning-disabled children (120).

Whey protein and N-acetylcysteine (NAC) can increase levels of glutathione which is necessary for detoxification and is depleted by toxic metals as previously noted (66). However care must also be exercised regarding proper level if these are supplemented, starting with low levels. Ensuring adequate calcium intake can reduce the toxic effects of lead (66). Chelation with chemical chelators such as DMSA can also greatly reduce metal body burden, but should only be considered with advice of a knowledgeable physician. DMSA (or EDTA) are effective for lead detoxification, but DMSA is also effective for mercury and other toxic metals. Studies have found that use of EDTA by patients with high levels of mercury can cause serious side effects, so EDTA should be used only when mercury levels have been found to be low or after reductions in mercury level using other means (170). DMPS is the most effective chelator for mercury body burden, but there have been some adverse effects that may be related to improper protocols. NAC, which can be obtained from most health food stores or catalogs, chelates mercury and arsenic but at a slower rate than the prescriptive chelators. Large numbers of children with ADD, autism, and other forms of learning disabilities have shown significant improvement after chelation and nutritional supplementation for deficiencies (23, 81d, 99, 130, 169a, 172, etc.) Common deficiencies found to also be a factor in such conditions are Omega-3 fatty acid (138), Vitamin B-6, lithium, zinc, iodine, and magnesium (46, 67-72, 75-78, 174, 597). In most such clinics treating these conditions, the majority improved after treatment (46, 48, 68-71, 75-78, 81, 113, 114, 115, 163, 169a, 172, 174).

Since metal toxicity causes hormonal imbalances and problems (155), tests for hormone levels of thyroid hormones, DHEA, cortisol, etc. are available (66de, etc.) and supplementation for such has been found effective for conditions such as ADHD (172, 66de). Other supplements that clinical studies have found often effective for ADHD include EFAs (DHA/EPA), phosphatidylserine, choline, DMAE, L-glutamine, B vitamins, magnesium, zinc, curcumin, sprirulina, DHEA, Iodine, Ginkgo biloba (172, 174, 176).

Avoidance of sugar and food allergens such as wheat gluten and milk casein, as well as regular exercise have also been found to be beneficial in treatment of ADHD (172, 169a).

Physical activity has been found to help kids who may be restless or hyperactive, or who have been *diagnosed with ADHD*[12]. Even emotional disturbances can be improved with exercise, as the activity provides an outlet for their energy and reduces the natural inclination of children to "act out." Use of exercise therapy along with Emotional Freedom Technique were found to have significant benefits (179). Exercise at school was also found to significantly increase reading and math ability of students, in addition to helping control obesity.

1.6 References

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